Iodine/iodide toxic reaction: case report with emphasis on the nature of the metabolic acidosis

ROLAND F. DYCK,* MD, FRCP[C]; ROBERT A. BEAR,† MD, FRCP[C], FACP; MARC B. GOLDSTEIN,† MD, FRCP[C]; MITCHELL L. HALPERIN,† MD, FRCP[C]

Complications that follow the ingestion of iodine or iodide or both have been described in a number of case reports and experimental studies,[1-4] and include gastrointestinal irritation and ulceration, chemical pneumonitis, hyperthyroidism, hemolytic anemia and acute renal failure due to tubular necrosis. In addition, metabolic acidosis has been described,[5] particularly in patients with burns treated with topical administration of povidone-iodine.[6] However, the nature of this metabolic acidosis has not been fully elucidated. In this report we describe a patient who ingested a large volume of Lugol's iodine (5% diatomic iodine and 10% potassium iodide) and subsequently manifested a clinical spectrum of toxic effects due to iodine/iodide. The metabolic acidosis was multifactorial in origin, resulting from acute lactic acidosis together with defects in hydrogen ion secretion in both proximal and distal nephron segments.

Case report

Clinical course and laboratory findings

A 56-year-old woman was admitted to hospital after attempting suicide by ingesting an unknown quantity of Lugol's iodine. The predominant gastrointestinal symptoms were due to esophagitis and gastritis and were characterized by marked throat and retrosternal burning. However, vomiting, diarrhea, clinical signs of paralytic ileus and occult blood in the stool were absent. Respiratory symptoms were limited to dyspnea.

She was alert and oriented; the blood pressure was 160/100 mm Hg when she was supine and 135/100 mm Hg when she was standing; the temperature was 36.8°C; the pulse rate was 120 beats/min and the rhythm regular; the jugular venous pressure was 7 cm of blood; the respiratory rate was 44/min; and there were bilateral inspiratory rales at the base of the lungs. The skin of the extremities was mottled but warm. Results of the rest of the general physical and neurologic examinations were normal.

The blood iodide value 6 hours after admission was 4.7 mmol/L (60 mg/dL). Initially the serum thyroxine value was 165 nmol/L (12.8 μg/dL) (normal 50 to 140 nmol/L [4 to 11 μg/dL]), but by 12 days after admission it had fallen to 122 nmol/L (9.5 μg/dL) and the tachycardia present since admission had disappeared. The hemoglobin value at the time of admission was 14.9 g/dL; by the third hospital day the value was 11.5 g/dL. A blood smear disclosed fragmented erythrocytes, and the proportion of reticulocytes was 3.0%. The bone marrow revealed normoblastic hyperplasia, compatible with the effects of hemolysis. Coombs' tests (direct and indirect) gave negative results. The cause for the anemia was not further evaluated. At the time of admission the urine had a specific gravity of 1.010 and contained erythrocytes, leukocytes and many hemegranular casts, which suggested acute tubular necrosis; at the time of discharge the results of urinalysis were normal. The serum creatinine value 24 hours after admission was 212 μmol/L (2.4 mg/dL); the value rose to 274 μmol/L (3.1 mg/dL) 7 days after admission, and then slowly fell to 106 μmol/L (1.2 mg/dL) 25 days after admission, consistent with the diagnosis of acute tubular necrosis.

A chest roentgenogram showed diffuse bilateral interstitial edema (Fig. 1). Dyspnea, hyperpnea, hypoxemia and roentgenographic evidence of interstitial pulmonary edema grad-

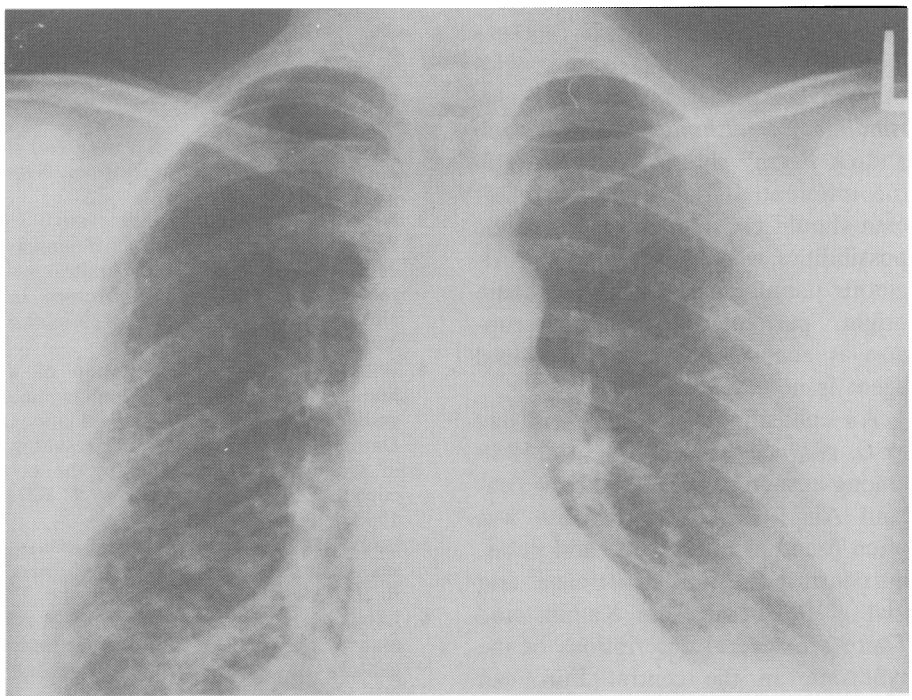

FIG. 1—Bilateral interstitial edema 24 hours after admission of patient with iodine/iodide toxic reaction.

From *the division of nephrology and the Gage Research Institute, Toronto Western Hospital, and †the division of nephrology, St. Michael's Hospital, Toronto

Reprint requests to: Dr. Robert A. Bear, Division of nephrology, Department of medicine, St. Michael's Hospital, 30 Bond St., Toronto, Ont. M5B 1W8

ually disappeared, and the arterial oxygen tension and chest roentgenograms were normal 4 days after admission.

The remainder of the laboratory results are shown in Table I.

Initially starch mucilage and sodium thiosulfate were given orally and isotonic sodium bicarbonate was administered intravenously. The sodium bicarbonate infusion was started about 4 hours after admission and was continued for the first 2 days; a total of 510 mmol was administered.

Acid-base data

Serial blood gas and electrolyte values following admission are detailed in Table I. The most striking early abnormalities included acidemia, a low serum bicarbonate concentration and a small apparent increase in the unmeasured anion gap. Since iodide causes the false impression of a disproportionate elevation in the serum chloride concentration when measured by autoanalyser techniques,[7,8] the calculated anion gaps in this patient were lower than the "true" values. This is exemplified by the data from samples obtained 6 hours after admission, when the serum iodide value was 4.7 mmol/L. The "true" anion gap corrected for iodide would be about 3 mEq/L higher than the calculated value at this time. In addition, the low serum albumin concentration (406 μmol/L or 2.8 g/dL) would also decrease the expected value for the anion gap by about 3 mEq/L.[9] Therefore, the elevation in the unmeasured anion gap should be (21 − 12) + 3 + 3 or 15 mEq/L, a value that closely approximated the serum lactate value (13 mmol/L). Therefore, the metabolic acidosis was in reality of the high unmeasured anion gap type and was due to lactic acidosis.

In simple metabolic acidosis of the unmeasured anion gap type, the rise in the unmeasured anion gap is roughly equal to the fall in the serum bicarbonate concentration. In this case, when the unmeasured anion gap was elevated by about 15 mEq/L, the serum bicarbonate concentration should have been depressed commensurately to about 10 mmol/L. That the serum bicarbonate value was much higher, 20 mmol/L, suggests that there was an additional source of bicarbonate present, presumably due to the sodium bicarbonate therapy.

The arterial carbon dioxide tension ($Paco_2$) in this patient at the time of admission was 24 mm Hg. This value was lower than expected on the basis of respiratory compensation for metabolic acidosis,[10] and led to the additional diagnosis of coexistent respiratory alkalosis. The respiratory alkalosis persisted for the first few days of hospitalization and was probably due to the chemical pneumonitis induced by the toxic effects of the iodine/iodide mixture.

The finding of an alkaline urine pH at a time when the plasma bicarbonate concentration was low suggests that the renal threshold for bicarbonate was reduced. This could be explained by the low blood $Paco_2$ or proximal renal tubular acidosis.[11-13] The finding of a reduced difference in carbon dioxide tension between the urine and the arterial blood when controlled for the urine bicarbonate concentration suggests that distal renal tubular acidosis may have been present,[14] or again it could reflect the low blood $Paco_2$.[15] The presence of renal tubular acidosis might indicate renal damage induced by the iodine/iodide mixture.

Discussion

The patient presented with a history of iodine and potassium iodide ingestion that led to esophagitis, gastritis, chemical pulmonary edema, transient hyperthyroidism, hemolytic anemia, acute tubular necrosis and several acid-base disturbances. In this report we documented that the metabolic acidosis associated with iodine/iodide ingestion was primarily due to lactic acidosis. We could not explain the lactic acidosis by factors such as sepsis, shock or hypoxia. Therefore, we suggest that lactic acidosis reflects a toxic effect of iodine/iodide that interfered in some way with adenosine triphosphate generation by oxidative metabolism. In a previously reported case a patient with burns received povidone-iodine and manifested metabolic acidosis. Unfortunately in that report the nature of the metabolic acidosis was not well defined.[6]

In summary, in this report we documented clinical features associated with an iodine/iodide toxic reaction. We observed that the acid-base disorder was in reality very complex. Understanding the influence of elevated serum iodide (or bromide) concentrations upon the unmeasured anion gap led to the early recognition of a significant elevation in the latter. A knowledge of the reciprocal relation between the unmeasured anion gap and the serum bicarbonate concentration enabled us to identify coexistent metabolic alkalosis. Using the 95% confidence band defining the relation between the serum bicarbonate concentration and the $Paco_2$ in metabolic acidosis, we were further able to diagnose primary respiratory alkalosis. Finally, appreciation of the relation between the concentration of

Table I—Laboratory data for patient with iodine/iodide toxic reaction

Variable	Time (h) after admission					
	0	3	6	17	24	48
Serum values of:						
Sodium (mmol/L)	135	135	142	138	139	139
Potassium (mmol/L)	6.6	5.7	3.8	3.6	3.2	3.2
Chloride (mmol/L)	104	109	101	100	105	102
Bicarbonate (mmol/L)	15	11	20	22	21	24
Iodide (mmol/L)	—	—	4.7	3.8	1.5	0.5
Lactate (mmol/L)	—	—	13	—	—	—
Anion gap (mEq/L)						
Calculated	16	15	21	16	13	13
True (estimated)	>16	>15	23-25	>16	—	—
Arterial blood values						
pH	7.38	7.37	7.45	7.51	7.50	7.50
Oxygen tension (mm Hg)	—	62	—	—	—	84
Carbon dioxide tension (mm Hg)	24	18	28	30	27	30
Urine pH	—	—	7.7	8.0	7.7	7.8
Urine CO_2 tension minus arterial CO_2 tension (mm Hg)	—	—	—	—	14	9

filtered bicarbonate and the urine pH led to the diagnosis of proximal renal tubular acidosis, while use of the difference in carbon dioxide tension between the urine and the arterial blood permitted us to suggest the presence of decreased hydrogen ion secretion in the distal renal nephron.

Dr. Dyck is a fellow of the Medical Research Council of Canada.

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